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Psychosocial Factors Predicting *BRCA1/BRCA2* Testing Decisions in Members of Hereditary Breast and Ovarian Cancer Families

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Although *BRCA1/2* testing has increasingly entered clinical practice, much is to be learned about the most effective ways to provide counseling to persons potentially interested in receiving test results. The purpose of this study was to identify factors affecting genetic testing decisions in a cohort of hereditary breast and ovarian cancer (HBOC) families presented with the choice to undergo testing. Relatives in these families are known to carry *BRCA1* or *BRCA2* mutations. Sociodemographics, personality traits, and family functioning were self-assessed using validated psychometric instruments at baseline. Among 172 individuals who participated in pretest education and counseling, 135 (78%) chose to undergo genetic testing and 37 (22%) chose not to be tested. Individuals who chose to undergo genetic testing were more likely to be older (≥40 years), to have lower levels of optimism, and to report higher levels of cohesiveness in their families. A better understanding of factors that influence interest in predictive testing may help to inform the counseling that occurs prior to genetic testing. Am. J. Med. Genet. 93:257–263, 2000.

KEY WORDS: *BRCA1/2* testing; hereditary cancer families; breast cancer; ovarian cancer; genetics education; genetic counseling; predisposition testing predictors

INTRODUCTION

Use of genetic testing to refine health risk predictions is a relatively new application of genome technologies. Much is to be learned about the most effective ways to offer predispostion genetic testing and to meet client needs. Much of our initial understanding of interest and utilization of predictive genetic testing comes from studies that have offered *BRCA1* and/or *BRCA2* testing to persons in hereditary breast and ovarian cancer families (HBOC). Other studies have shown that members of HBOC families who undergo education and counseling, more often than not, choose to be tested [Lerman et al., 1996; Botkin et al., 1998]. Women were shown to be more interested in testing than men [Lerman et al., 1996]. In this article, we sought to identify sociodemographic, psychological, and family variables that characterize members of HBOC families who are more likely to choose to undergo predictive testing following pretest education and counseling. We predicted that those who had been affected with cancer (specifically breast and ovarian cancer) or were closely related to those who had been affected would be more likely to choose genetic testing. We also predicted that women would be more likely to undergo testing than men because the cancer risks associated with carrying a mutation involve primarily women. Further, we predicted that higher self-esteem, optimism, and spirituality would also predict interest in genetic testing. Overall, these predictions were based on our clinical experience and on previous research results [Biesecker et al., 1993; Struewing et al., 1995; Lerman et al., 1996].

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METHODS

Study Population

The participants in this study were 172 adult (≥18 years old) men and women in families previously enrolled in a familial cancer study by the National Cancer Institute [Struewing et al., 1995]. Those under 18 were excluded. All participating families had a risk-conferring mutation in *BRCA1/2* and at least (a) two cases of ovarian cancer in first-degree relatives, or (b) three cases of breast cancer and at least one case of ovarian cancer, or (c) at least four cases of breast cancer.

Study Protocol

All members of the NCI extended families in which a *BRCA1* or *BRCA2* mutation was identified were invited to participate in an education and counseling study that introduced genetic testing as a personal choice. Members of the same family were sent an invitation letter simultaneously unless there were no means to contact them, in which case we relied on relatives to contact them. At the initial visit and prior to pretest education and counseling, participants completed a questionnaire that included assessment of sociodemographic and psychological factors and family functioning. Following this baseline assessment, individuals participated in a family group (usually less than five persons simultaneously present) pretest education session, and a subsequent individual counseling session. The education session was standardized (scripted) and accompanied by slides. It addressed the topics of breast and ovarian cancer incidence, cancer risk factors, contribution of predisposing gene mutations, description of hereditary breast and ovarian cancer, risks associated with *BRCA1* or *BRCA2* mutations, pros, cons, and limitations of genetic testing, cancer screening options, and breast self-examination. A research nurse with experience in oncology taught most of the education sessions. Infrequently, they were taught by a genetic counselor.

Participants were randomized for the type of individualized counseling they received. Counseling was either a provider-driven problem solving or a client-centered style, each intended to facilitate decision making about genetic testing. Board-certified genetic counselors (n = 3), a physician with expertise in cancer epidemiology (n = 1), or research nurses (n = 2) provided the individualized counseling. The counseling sessions were limited to 1 hr. Although all participants were randomized to receive one of two counseling approaches, there were no differences in genetic testing uptake between the two groups. Therefore, the data are combined for all analyses that follow.

Description of Interventions

The client-centered intervention was modeled after common practices in genetic counseling that surround decision making for genetic testing. The intervention involved several open-ended questions with probes to address the most significant areas of concern for the client. It also included hypothetical inquiry into the possible outcomes of choosing or not choosing testing as well as the possible outcomes of receiving either test result. These sessions were intended to follow the lead of the client but were guided by a structured outline for some consistency.

The problem-solving intervention, on the other hand, was led by the counselor. Problem-Solving Training is a cognitive–behavioral intervention that teaches people to select and implement the most effective coping strategies for a given stressor [D'Zurilla, 1988]. It was applied to those choosing genetic testing under the assumption that the decision whether to undergo testing was a stressor. If clients felt they already had made a decision, then they were encouraged to choose a problem that may arise in carrying out the decision. The protocol included problem definition, generation of solutions, solution evaluation, decision making, and solution implementation. The goals of this intervention were not only to facilitate test decision making but also to teach clients effective strategies for coping with stress in the future. Problem solving was facilitated by the use of a flip chart and a worksheet that was given to clients. Providers involved in the study underwent training in administering the intervention in order to standardize delivery.

Test Decisions

After the individual counseling session, all participants were presented the option of whether to undergo *BRCA1/2* testing. Participants who were ambivalent about their decision that day were given the option of being tested at a later date. Several participants delayed their decision but were included in the analysis as tested as they decided to go forth and receive their results. Those who chose not to undergo testing by the conclusion of the study were considered nontesters. Two people who had blood drawn but chose not to receive their test results were also considered nontesters. All testing, education, and counseling were provided through the National Institutes of Health (NIH) at no charge.

Mutational Analysis

Originally, *BRCA1* or *BRCA2* mutations were identified in affected members of these HBOC families on a research basis. This follow-up testing protocol was designed so that those who chose testing had a blood sample drawn specifically for this purpose and sent to a NIH research laboratory as well as to a CLIA-approved laboratory for separate confirmation of the mutation known to be present in each family. All Ashkenazi Jewish participants also were tested for the three most prevalent *BRCA1/2* mutations in that ethnic population [Brody and Biesecker, 1998].

Measures

Sociodemographics. Data on gender, age, education, employment status (full-time, part-time, unemployed, retired), and marital status (never vs. ever married) were gathered.

Clinical information. Date were gathered on cancer status, family history (presence of first-degree relatives with breast or ovarian cancer) and number of

years in research (none, >0). Cancer diagnoses were confirmed by pathology reports.

Psychosocial variables. Data were gathered on family relationships, depression, spirituality, self-esteem, and optimism/pessimism. Dimensions of family relationships; conflict, cohesion, and expressiveness were assessed using the family relationship index, a subscale of the Family Environment Scale (FES). The FES is a 90-item survey on self-perception of the nuclear family environment [Hoge et al., 1989; Moos and Moos, 1994]. The FES was found to have acceptable test-retest reliabilities (0.68–0.86) with numerous studies supporting its construct and discriminant validity in various populations [Moos and Moos, 1994].

The Center for Epidemiologic Studies Depression (CES-D) Scale was administered to assess depressive symptomatology. The CES-D has adequate test-retest reliability ($r = 0.57$ for 2–8 weeks) and was shown to relate to clinical ratings of the severity of depression [Radloff, 1977]. Possible scores on this measure range from 0 to 60, with higher scores reflecting more depressive symptoms. The Cronbach's alpha coefficient for our sample was 0.79.

Personal spiritual meaning and satisfaction was assessed using the Spiritual Well-Being Scale (SWBS). This scale is a 20-item self-report that was validated widely with respect to both religious and existential well being [Ellison and Smith, 1991]. The highest possible score of overall spiritual well being is 120, with higher numbers representing greater well being. In a previous study of well being in women undergoing treatment for gynecologic cancers, the test-retest reliability coefficient was 0.93 for total well being [Gioiella et al., 1998]. The Cronbach's alpha coefficient for our sample was 0.85.

Global self-esteem was assessed using the Rosenberg Self-Esteem Scale. It is a 10-item scale designed as a global measure of self-esteem [Rosenberg, 1965]. Scores are collapsed into six scoring categories so that total scores range from 0 to 6. Higher self-esteem is reflected in scores of 0–2 and low self-esteem in scores of 3–6. Curbow and Somerfield report Cronbach's alpha coefficients ranging from 0.76 to 0.87 and a test-retest reliability of 0.74 [Curbow and Somerfield, 1991].

Dispositional optimism was assessed by administering the brief Life Orientation Test (LOT). The brief LOT is a 10-item, Likert-style questionnaire that measures the level of optimism in one's outlook on life [Scheier et al., 1994]. An optimism score is created by summing six items; a higher score indicates a more optimistic outlook. This scale was shown to have a test-retest reliability of 0.74 [Carver et al., 1994]. The Cronbach's alpha coefficient for our sample was 0.38.

Testing Decision

Participants were classified as either choosing or not choosing to undergo *BRCA1/2* testing. Those who chose to undergo testing received their test results in person 2–6 months following testing.

Statistical Analysis

Mantel-Haenszel χ^2 tests of association were performed for categorical variables to identify sociodemographic predictors of uptake of genetic testing. The Student's *t*-test was used to assess the association of testing decision with continuous variables, such as the psychosocial measures. Logistic regression models using general estimating equations were used to evaluate the association of sociodemographic and psychosocial measures with genetic testing decision. All tests of statistical significance were two-sided. Demographic and psychosocial measures having univariate associations ($P < 0.1$) with the decision to undergo genetic testing were included in the multivariate analysis. Those variables accounting for a significant amount of the variance were retained in the final model. Counseling style was also included in the final model as a controlling variable. Analyses were performed using PROC T-TEST, PROC FREQ, or PROC GENMOD in Windows-based SAS Version 6.12 (SAS Institute Inc., Cary, NC).

RESULTS

Genotype Results

The *BRCA1* mutations present in the 11 families included in this analysis were 185delAG, C61G, 1294del40, 3600del11, 5256delG, and 5382insC. The BRCA2 mutation is 6174delT.

Characteristics of the Study Population

Two hundred forty-four eligible relatives were invited to participate in an education and counseling study in which predictive testing would be offered. One hundred twelve (46%) were male and 132 (54%) were female. Letters were followed with a personal telephone call unless eligible relatives returned a postcard asking that they not be recontacted.

Of the 172 individuals participating in the education and counseling sessions, 135 (78%) chose to undergo testing and 37 (22%) chose not to be tested. Of the 172 participants, the median age was 40, 110 (64%) were women, and 62 (36%) were men. All participants in the study were Caucasian. Fifty-one (30%) participants identified themselves as single, divorced, separated, or widowed and 121 (70%) as married. One hundred twenty-four (72%) individuals were employed; half of the remaining 28% were retired. There was a wide range of annual income reported: 20 participants (12%) with less than $20,000 and 24 (28%) with greater than $75,000. Fourteen participants (8%) were affected by breast or ovarian cancer themselves and 70 (41%) had at least one first-degree relative affected with cancer. Sixty-one (38%) participants had never participated in research (although members of their extended family did, making them eligible to participate) whereas 101 (62%) were previous research participants. There were 38 nuclear families in which both a parent and child(ren) participated. Of these families, 26 were concordant in their choice whether or not to be tested.

Bivariate Analysis

Sociodemographic and clinical traits that serve as predictors of genetic testing decisions are summarized in Table I. Age and marital status were significantly associated with genetic testing decisions, where older

(≥40 years of age) and married participants were more interested in undergoing testing. In contrast, those tested did not significantly differ from those who chose not to undergo testing by gender, cancer status, or by the presence of first-degree relatives affected with cancer. Furthermore, they did not differ with regard to the type of counseling they received, the number of years of prior research participation, or the research site (NIH vs. a field clinic setting).

Summarized in Table II are the psychosocial predictors of *BRCA1/2* testing. Greater family cohesion (as measured by the Family Environment Scale) and dispositional optimism were statistically significant predictors of the decision to undergo genetic testing. Family conflict, family expressivity, depression, spirituality, and self-esteem levels were not associated with the genetic testing decision.

Multivariate Analysis

Variables that were significant in the bivariate analysis were tested in a logistic regression model summarized in Table III. Family cohesion, optimism, and age continued to be independent predictors of testing. The adjusted odds ratios were 1.05 (95% CI 1.01–1.08), 0.87 (95% CI 0.79–0.95), and 3.12 (95% CI 1.32–7.36), respectively. Marital status failed to independently predict the decision whether to undergo genetic testing.

DISCUSSION

Of the 244 eligible relatives we contacted by letter and telephone, 55% chose to participate in the education and counseling study and to have *BRCA1/2* testing. This rate resembles the 43% uptake rate reported by Lerman et al. [1996] in a study of 279 relatives within similar extended HBOC families. Participants in their study had undergone consent and a baseline telephone interview, but genetic education occurred later when participants could also receive their test results. Of the HBOC relatives who completed a baseline survey and participated in an education and counseling session, 78% chose to be tested and to receive their results. This exceeds the uptake rate of 54% rate reported by Smith et al. among members of a similar extended HBOC family who had undergone consent, a baseline interview, and genetic counseling [Smith et al., 1999]. Our uptake rate among relatives who received education and counseling may overrepresent actual testing rates in HBOC families because relatives who were not interested in testing likely chose not to participate in the study. Traveling to the NIH or even to a field clinic in order to participate may have deterred those who were ambivalent about testing.

Before testing was possible, Struewing et al. [1995] reported that that 79% of participants in the same population would definitely want to be tested and that 16% would probably want to be tested. We are not aware of any eligible relative who was tested outside of this study. Our figures for actual uptake are lower than might be predicted by this previous interest survey. However, within a variety of health decision making, such as predictive genetic testing, people's intentions or attitudes often do not simply predict their behaviors, with interest often exceeding uptake [Ajzen and Madden, 1986; Ajzen and Madden, 1991]. Once participants understand and assimilate the potential outcomes of testing, fewer undergo testing. Our findings are consistent with this trend and in particular with past experience in offering presymptomatic testing for Huntington disease (HD) where uptake was less than predicted based on studies of interest in at-risk relatives [Wiggins et al., 1992]. However, it is notable that the uptake in the at-risk HD population was substantially lower (11–15%) [Craufurd et al., 1989; Wiggins et al., 1992]. It is likely that we are demonstrating differences in testing uptake that may be based on the condition involved and its perceived likelihood for being treatable or preventable.

Based on previous clinical experience in counseling members of HBOC families, we anticipated that the elders in these HBOC families would be more likely to choose genetic testing. Our findings demonstrate that age is the strongest predictor of the decision to undergo testing. The matriarchs and patriarchs of HBOC fami-

TABLE I. Demographic and Clinical Predictors of *BRCA1/2* Testing

Predictor	Level	*N*	Tested *N* (%)	Chi-square	*P* value
Demographics					
Sex	Female	110	87 (79%)		
	Male	62	48 (77%)	0.07	0.80
Age	≤40 years	87	63 (72%)		
	>40 years	85	72 (85%)	3.85	0.05
Marital status	Married	121	101 (84%)		
	Single	51	34 (67%)	6.00	0.014
Clinical					
Cancer	No	96	76 (79%)		
Status[a]	Yes	14	11 (79%)		0.99[b]
FDRs	No	102	83 (81%)		
	Yes	70	52 (74%)	1.24	0.27
Counseling style	Client	93	75 (81%)		
	Provider	78	60 (77%)	0.35	0.55
Years in research	None	61	47 (77%)		
	>0	101	81 (80%)	0.23	0.63

[a]Restricted to women participants.
[b]Fisher's exact.

TABLE II. Psychosocial Predictors of *BRCA1/2* Testing

Predictor	Level	Tested (*SD*)	Not Tested (*SD*)	*t*-test	*P* value
Family relations index	Conflict	43.7 (8.6%)	44.3 (10.1)	–0.323	0.75
	Cohesion	56.9 (11.4)	51.0 (16.9)	1.972	0.05
	Expressiveness	54.4 (12.4)	53.3 (13.5)	0.437	0.66
Depression		7.3 (6.6)	6.9 (6.8)	0.307	0.76
Spirituality		95.4 (20.3)	96.9 (18.8)	–0.412	0.68
Self-esteem		26.2 (1.9)	26.5 (1.5)	–0.942	0.35
Optimism		30.2 (5.1)	32.1 (5.1)	–1.968	0.05

lies may have less concern about their own risks of developing cancer but more concern about risks to their adult children or grandchildren. Age as a predictor of testing is not unexpected in this population because previous research in HBOC families showed that one of the strongest motivations for wanting to be tested is to learn about risks to ones' children [Lerman et al., 1994; Struewing et al., 1995; Lerman et al., 1996]. This also was reported in Huntington disease families [Evers-Kiebooms et al., 1989]. It is reasonable that within families an elder may decide to be tested before proceeding to the next at-risk generation. Our study was not designed to offer testing first to elders, thus these decisions were made freely by individuals or family groups. Within 38 nuclear families where both parent and child(ren) participated, the choice whether to be tested was concordant in 26 (68%) families. Although this suggests there is family influence on the testing choice, a predictive pattern of family testing was not captured beyond age.

Studies of other HBOC families suggest that women are more likely to pursue *BRCA1/2* testing [Lerman et al., 1996]. This is consistent with our expectations because women are at substantially increased risk for cancer if they carry a gene mutation. In this study, however, sex was not a predictor of test decision. Because age was such a strong predictor, older men with daughters and granddaughters were apparently as motivated as the matriarchs to choose testing despite their relative difference in cancer risk.

We also hypothesized that being affected with breast or ovarian cancer or being closely related to affected relatives would motivate people to want confirmation of the presence or absence of an underlying mutation. Family history was correlated with uptake or interest in genetic testing in previous studies [Issacs et al., 1996; Lerman et al., 1996]. Neither of these hypotheses was supported by the data because we found no differences between those that chose testing and those individuals who did not. Within these HBOC families, cancer did not serve as a significant motivator for seeking an explanation or learning about potential additional cancer risks. Additionally, proximity to those affected in the extended family did not differentiate those who chose testing. Because this contradicts other research findings, the relative importance of having close relatives affected with cancer in making a decision to pursue genetic testing remains unclear. This has implications for genetic counseling because counselors might reasonably make prior assumptions about clients' decisions based on cancer history.

TABLE III. Logistic Regression Analysis of *BRCA1/2* Testing

Variable	Odds ratio (95% CI)
Family Cohesion	1.05 (1.01–1.08)[a]
Optimism	0.87 (0.79–0.95)[a]
Age (40 years as the median)	3.12 (1.32–7.36)[a]
Marital status (married or not)	0.76 (0.31–1.92)
Counseling style	1.01 (0.44–2.31)

CI, confidence interval.
[a]Significant at $P < 0.05$.

The lack of a difference in uptake demonstrated by counseling style suggests that participants' decisions whether to undergo testing is not influenced by the styles of counseling used in this study to support their decision making. Analysis of the long-term outcomes of this study should determine whether there were other differences in counseling outcomes or potential benefits of either approach. Further, seeing a significant proportion of participants in field clinics closer to their homes also did not affect the choice to be tested. It seems that convenience was not a significant factor in pursuing testing among members of these HBOC families.

Evaluation of the psychological assessment at baseline may provide insights into personal motivations for testing. Understanding personality traits and coping resources for those facing choices about genetic testing may enhance the effectiveness of pretest genetic counseling by identifying reasons that make it more likely that someone would choose testing. We found that participants with dispositional optimism were less likely to choose testing. Prior research suggests several reasons why optimists may be less likely to undergo testing.

Optimists may overestimate the chance that they did not inherit the gene mutation in the family or they may underestimate the chances that they will develop cancer [Alloy and Aherns, 1987]. This effect is layered upon the tendency to generally be unrealistically optimistic that events interpreted as "positive" will happen to them and that events interpreted as "negative" will not [Scheier and Carver, 1992, 1993]. Further, optimists were shown to be more capable of coping with stressful life events [Scheier and Carver, 1986] by employing strategies that allow them to accept and adapt to anxiety-producing circumstances. In this case, participants who are optimists are more likely to accept the possibility that they may have a higher cancer risk and/or a chance of passing the family mutation on to their children without feeling motivated to further clarify their risk through testing. This is consistent with previous research that indicated that disposi-

tional optimists are more likely to take risks [Norem and Cantor, 1986]. Although optimists are less likely to undergo testing, we have yet to learn whether there are differences in how they cope with not having test results.

Our study also determined that participants from cohesive families are more likely to choose testing. Previous research on cohesive families suggested that they are generally more resilient to stressful life events such as breast cancer [Friedman et al., 1988; Morse and Fife, 1998]. Cohesive families had better outcomes when a child had a chronic condition or dies [Henggeler et al., 1990]. Further, family cohesion was associated with better diabetic control and with pursuit of health-promoting behaviors [Marteau et al., 1987; Hanson et al., 1995; Ford-Gilboe, 1997]. Cohesion measures an amount of support and shared intimacy that provides a resource for anxiety-producing events. Thus, it is not surprising that participants from cohesive families were more likely to choose genetic testing. We anticipate that they will also prove to be more resilient to receiving mutation carrier test results and to related stress upon the assessment of our outcome measures.

STUDY LIMITATIONS

One potential criticism of studying families that have previously participated in NCI research is the potential lack of ability to generalize the results, even to other HBOC families. Some members of these extended families had not participated in the first epidemiological investigation (and many knew nothing of it) so we could compare those that had previously participated in research, some for as long as 20–25 years, to those that had never previously participated in research. Previous participation in NIH studies did not predict the decision to undergo testing. These are interesting results because we anticipated that the motivation to "help" the course of research might influence a participant's choice to undergo a clinical genetic test. These data contradict the suggestion that the longer people have been participating in research the more likely they may be to choose *BRCA1/2* testing, and imply they are capable of making personal decisions in a research setting.

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